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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,339	01/25/2002	Teddy Kosoglou	CV01490K	1512

24265 7590 03/01/2006

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER

20060215

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This is in response to the communication filed on Jan 31 2006 by the Board of Patent Appeals and Interferences.

As requested by the BPAI,

(1) The Information Disclosure Statements (IDSS) filed on August 26, 2002, and August 21, 2002 by the applicant have been considered.

(2) The complete articles of the following prior art references cited on page 3 of the September 9, 2005 Examiner's Answer are sent along with this communication.

Chobanian, Aram.V. "Antiatherogenic Effect of Captopril in the Watanabe Heritable Hyperlipidemic Rabbit", Hypertension 1990, 15(3), pp 327-331.

Schaarmann, G. "Influence of Soluble Dietary Fibre on the Faecal Excretion of Tocopherol and Blood Lipids in Women" Nutrition Research, 1999, 19(5), pp. 689-695.

Myasnikov, A. L. "Influence of Certain Vitamins on Cholesterolemia and the Development of Experimental Atherosclerosis" Klin. Med. U.S.S.R. 1950, 28(2), pp. 3-10.

Lelek, I. "Effect of Essential Fatty Acids on the Plasma Lipoprotein Fractions in Experimental Atherosclerosis" Orvosi Hetilap 1960, 101, pp. 1735-1738.

(3) A supplemental Examiner's Answer which complies with the new rules under 37 CFR 41.37 (c) is included.

The application has been forwarded to the Board of Patent Appeals and Interferences for decision on the appeal.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 7.30am-3.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/057,339
Filing Date: January 25, 2002
Appellant(s): KOSOGLOU ET AL.

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SUPPLEMENTAL EXAMINER'S ANSWER

This is in response to the appeal brief filed 06/15/2005

(1) Real Party in Interest

A statement identifying the real party of interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The statement of the status of amendments after final rejection contained in the brief is correct. No claims were amended after final rejection.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the issues in the brief is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 5,846,966 Rosenblum et al. 12-1998

Chobanian, Aram.V. "Antiatherogenic Effect of Captopril in the Watanabe Heritable Hyperlipidemic Rabbit", Hypertension 1990, 15(3), pp 327-331.

Schaarmann, G. "Influence of Soluble Dietary Fibre on the Faecal Excretion of Tocopherol and Blood Lipids in Women" Nutrition Research, 1999, 19(5), pp. 689-695.

Myasnikov, A. L. "Influence of Certain Vitamins on Cholesterolemia and the Development of Experimental Atherosclerosis" Klin. Med. U.S.S.R. 1950, 28(2), pp. 3-10.

Lelek, I. "Effect of Essential Fatty Acids on the Plasma Lipoprotein Fractions in Experimental Atherosclerosis" Orvosi Hetilap 1960, 101, pp. 1735-1738.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 22-23, 33-34 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (5,846,966) in view of Chobanian et al. 112CA: 151588, 1990.

Rosenblum et al teach the claimed cholesterol absorption inhibitors instantly claimed compounds of Formula (I), such as ezetimibe compound as old and well known in combination with another therapeutic cardiovascular agent such as cholesterol biosynthesis inhibitor, and with various pharmaceutical carriers and excipients in a dosage form (see column 32, example 6). This medicament is taught as useful for reducing cholesterol and for treating vascular condition such as arteriosclerosis (column 4, lines 50-66), at those levels herein envisioned (see column 20, line 21). Rosenblum further teaches that the risk factors associated for atherosclerotic coronary heart disease, include hypertension, serum cholesterol etc. See column 1, lines 26-30. It is also taught that the pharmaceutical composition comprising compound of formula (I) can be prepared using conventional excipients, and additives which include non-toxic compatible fillers, binders, disintegrants, buffers, preservatives, anti-oxidants, thickners, emulsifiers etc. See column 21, lines 5-15.

Chobanian et al. teach the claimed cardiovascular agent, captopril as old and well known in combination with various pharmaceutical carriers and excipients, in a dosage form (see abstract). This medicament is taught as useful for treating hypertension, and arteriosclerosis, at those levels herein envisioned.

Claims 1, 3, 22-23, 33-34 and 49, and the primary references, differ as to:

1) the concomitant employment of these medicaments.

It is generally considered prima facie obvious to combine two, or more, compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional anti-arteriosclerosis agents. It would follow that the recited claims define prima facie obvious subject matter. Cf. *In re Kerhoven*, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claim 49 specifically requires a pharmaceutical composition for various therapeutic uses. Examiner cited prior art employed the claimed compounds for various vascular therapeutic uses, not specifically reciting other uses for the formulation.

Applicant's attention is drawn to In re Dillon, 16 USPQ2nd 1897 at 1900 (CAFC 1990). The court sitting in banc ruled that the recitation of a new utility for an old and well known composition does not render that composition new.

Claims 43-46 are rejected under 35 U.S.C.103(a) as being unpatentable over Rosenblum et al (966), and Chobanian et al. as applied to claims 1, 3, 22-23, 33-34 and 49 above, and further in view of Lelek et al, Myasnikov, and Schaarmann et al.

Lelek et al teach the claimed omega 3 fatty acids, (linolenic acid) as old and well known in combination with various pharmaceutical carriers and excipients in a dosage

form. This medicament is taught as useful for reducing cholesterol and treating arteriosclerosis at those levels herein envisioned.

Myasnikov teaches the claimed vitamin C as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. This medicament is taught as useful for reducing cholesterol and treating arteriosclerosis, at those levels herein envisioned.

Schaarmann et al teach the claimed soluble fiber as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form (see abstract). This medicament is taught as useful for positively influencing the ratio of HDL to LDL ratio, and thereby constructively reducing the cholesterol level and treating arteriosclerosis.

Claims 43-46, and the primary references, differ as to:

1) the concomitant employment of these medicaments

It is generally considered prima facie obvious to combine two, or more, compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional anti-arteriosclerosis agents. It would follow that the recited claims define prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 43-46 specifically requires a pharmaceutical composition for various therapeutic uses. Examiner cited prior art employed the claimed compounds for various vascular therapeutic uses, not specifically reciting other uses for the formulation.

Applicant's attention is drawn to *In re Dillon*, 16 USPQ2nd 1897 at 1900 (CAFC 1990). The court sitting in banc ruled that the recitation of a new utility for an old and well known composition does not render that composition new.

(10) Response to Argument

Claim Rejections- 35 U.S.C. 103(a) Maintained

Claims 1, 3, 22-23, 33-34 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,846,966) in view of Chobanian et al.

Appellant argues that "Rosenblum et al. do not suggest or disclose a combination of a compound of formula (I) with a cardiovascular agent selected from the group consisiting of channel blockers, adrenergic blockers, adrenergic stimulants, angiotensin-converting enzyme (ACE) inhibitors, antihypertensive agents, angiotensin II receptor antagonists, anti-anginal agents, coronary vasodilators, diuretics and combinations thereof." See page 9 of the Brief.

In response, it is noted that Rosenblum teaches a combination of cholesterol absorption inhibitor with other therapeutic agents such as cholesterol biosynthesis inhibitors, for the treatment of atherosclerosis. It is noted that the basis of the rejection is the fact that the herein claimed agents i.e the composition of Rosenblum et al., Chobanian et al. is well-known to be useful for reducing the risk of atherosclerosis individually. Therefore, it flows logically to combine these agents together, which is taught by the prior art to be useful for the same purpose, in order to formulate a single composition useful for the same purpose. See *In re Kerkhoven* 205 USPQ 1069. Such a

composition not only treats hypertension, but also reduces cholesterol, and thus will have better atherosclerosis effect.

Appellant argues that "even if Chobanian et al. can be said to teach the use of captopril for the treatment of atherosclerosis, which Applicants do not concede, it can also be said to teach away from the concept of use of two separate compounds (a compound of formula (I) and a separate cardiovascular agent as claimed) because captopril would serve both functions as an antihypertensive and a treatment for atherosclerosis." See page 10 of the Brief.

In response, it is noted that the outstanding rejection is an obviousness rejection and Chobanian is only one of the two cited prior arts. Therefore, Chobanian alone would not be teaching such combination. The basis of the rejection is that the compositions, of Rosenblem et al. and Chobanian are known to be useful in treating atherosclerosis. Further, Rosenblum teaches that compounds of formula (I) of the instant invention can be combined with other therapeutic agents, and also teaches that hypertension, and serum cholesterol are the risk factors of atherosclerosis. Thus, one of ordinary skill in the art would have been motivated to use two separate compounds each of which are taught individually for reducing the risk of atherosclerosis in a single composition.

Appellant argues that "Contrary to the assertions in the Office Action, the Final Office Action and the Advisory Action, the desirability of combining of the two categories of compounds, and a suggestion that the combination of the two categories of compounds would actually work together, is not shown in the references." See page 10 of the Brief.

In response, it is noted that Rosenblum et al. teach that hypertension, and serum cholesterol are the risk factors for atherosclerotic coronary heart disease. Rosenblum

teaches that instantly claimed compounds are used for lowering serum cholesterol, and treatment of atherosclerosis. Chobanian teaches that captopril is used in the treatment of hypertension, and atherosclerosis. See page 331, left column, lines 19-22. Thus, from the teachings of Rosenblum, and Chobanian it would have been obvious to a person of ordinary skill in the art at the time of invention to combine instantly claimed compounds such as ezetimibe with captopril with the expectation of at least obtaining an additive effect in reducing the risk of atherosclerosis.

Appellant argues that "combining the Rosenblum et al. and Chobanian et al. references renders the present claims at best "obvious to try", which is not the standard for patentability." See page 11 of the Brief.

In response, it is noted that "there is nothing to try for". *In re Fritch* as cited by appellant is misplaced in the instant situation. In *In re Fritch* the claimed invention possesses feature not taught or suggested by the references i.e "overall flexibility and landscape retention function". In the instant situation the cited references teach or suggest all the functions herein, i.e Rosenblum teaches that instantly claimed compounds are used for lowering serum cholesterol, and treatment of atherosclerosis. Chobanian teaches that captopril is used in the treatment of hypertension, and atherosclerosis. Thus, from the teachings of Rosenblum, and Chobanian it would have been obvious to a person of ordinary skill in the art at the time of invention to combine instantly claimed compounds such as ezetimibe with captopril with the expectation reducing the risk of atherosclerosis with at least additive effect..

Claims 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,846,966) in view of Chobanian et al. as applied to claims 1, 3, 22-23, 33-34, and 49 above, further in view of Lelek et al., Myasnikov and Schaarmann et al.

Appellant's arguments on pages 14, and 15 paragraph 1 are essentially the same as that presented in pages 9-10 which are addressed above.

Appellant argues that "Schaarmann et al. teach that high intake of dietary fiber does not deteriorate the absorption of tocopherol (vitamin E) in women. The relevance of this statement to treatment of atherosclerosis with the combination of compounds currently claimed is tenuous, at best." See page 15 of the Brief.

In response, it is noted that Rosenblum et al. teach that hypertension, and serum cholesterol are the risk factors for atherosclerotic coronary heart disease. Rosenblum teaches that instantly claimed compounds are used for lowering serum cholesterol, and treatment of atherosclerosis. Schaarmann teaches that the claimed soluble dietary fiber is used for increasing the concentration of HDL-cholesterol (good cholesterol) and at the same time decreasing the LDL-cholesterol (bad cholesterol) concentration, thus significantly improving the LDL-/HDL-cholesterol ratio. See page 694. Thus, from the teachings of Rosenblum, Chobanian, and Schaarmann, it would have been obvious to a person of ordinary skill in the art at the time of invention to combine instantly claimed compounds such as ezetimibe, captopril with dietary fiber with the expectation of at least obtaining an additive effect in reducing the risk of atherosclerosis.

Appellant's argument in page 16 of the Brief is that "Lelek et al. and Myasnikov do not teach or suggest the use of the compounds described therein, in combination with any other compounds, nor the combination of compounds specifically claimed in Claim 1."

Examiner notes that the basis of the rejection is the fact that the herein claimed agents i.e the compositions of Rosenblum, Chobanian, Lelek et al. and Myasnikov are well known to be useful for reducing the risk of atherosclerosis individually, and it is also noted that Rosenblum teaches that pharmaceutical compositions comprising compound of Formula (I) can be prepared using conventional excipients and additives which include non-toxic compatible fillers, binders, disintegrents, buffers, preservatives, anti-oxidants, etc. Therefore, it flows logically to combine these agents together, which is taught by the prior art to be useful for the same purpose in different mix-and-match manner, in order to formulate a single composition useful for the same purpose. See *In re Kerkhoven* 205 USPQ 1069. Such a composition would at least expect additive effect in reducing the risk of atherosclerosis.

Appellant argues in page 16 of the Brief "As noted above in the discussion of the previous rejection, there is no way to know, absent testing, whether combinations of compounds having completely different mechanisms of action will actually work as expected. Applicants respectfully submit that the combination of three compounds as claimed in Claims 43-45 is not obvious in view of the references cited. There is simply no suggestion or evidence that the compounds will work together as asserted in the Office Action".

In response, the basis of the outstanding rejection is that the claimed agents are known to useful for reducing the risk of atherosclerosis. The motivation to combine is not because of their mechanisms of action. Therefore, absent to the contrary, it flows

logically to combine these agents together, which is taught by the prior art to be useful for the same purpose, in order to formulate a single composition useful for the same purpose. See *In re Kerkhoven* 205 USPQ 1069. Such a composition would at least expect additive effect in reducing the risk of atherosclerosis.

Appellant's argument in page 17 of the Brief that "Applicants respectfully assert that the rejection is based upon Improper hindsight reconstruction and respectfully request that the rejection of claims 43-46 under 35 U.S.C. 103(a) be reconsidered and withdrawn."

For the same reasons as discussed above, said claims are properly rejected under 35 U.S.C.103(a).

For the above reasons, it is believed that the rejections should be sustained.

(11) Related Proceedings Appendix
None

Respectfully submitted,

Shobha Kantamneni
February 15, 2006

Conferees

Sreeni Padmanabhan
Wang, Shengjun

SHENGJUN WANG
PRIMARY EXAMINER

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